



AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph at page 19, lines 18 to 33 as follows:

Preferably, the one or more primers used is an oligonucleotide including one or more nucleotides of random sequence. More preferably, the one or more primers is an oligonucleotide including one or more contiguous nucleotides of random sequence. More preferably, the one or more of primers is an oligonucleotide that includes six or more contiguous nucleotides of random sequence, such as a DOP primer (degenerate oligonucleotide primer). Most preferably, the one or more primers is a primer with the following nucleotide sequence:

5'-CCGACTCGAGNNNNNATGTGG-3';

5'-CCGACTCGAGNNNNNATGTGG-3' (SEQ ID NO.1);

where NNNNNN represents the degenerate sequence. "N" is any nucleotide ie N represents the four possible nucleotides in the DNA sequence: "A", "T", "C" and "G" for Adenine, Thymine, Cytosine and Guanine, respectively. As such, the degenerate sequence contain mixtures of various nucleotide sequences including all possible combinations of A, T, C and G at the "N" positions.

Please replace the paragraph beginning at page 27, lines 24 to 33 to page 28, line 5 as follows:

Preferably, the one or more of the primers used for amplification is an oligonucleotide including one or more nucleotides of random sequence. More preferably, the one or more primers is an oligonucleotide including one or more contiguous nucleotides of random sequence. More preferably, the one or more of the primers is an oligonucleotide that includes six or more contiguous nucleotides of random sequence, such as a DOP primer (degenerate oligonucleotide primer). Most preferably, the one or more primers is a primer with the following nucleotide sequence:

~~5'-CCGACTCGAGNNNNNATGTGG-3'~~

5'-CCGACTCGAGNNNNNATGTGG-3' (SEQ ID NO.1);

where NNNNN represents the degenerate sequence. "N" is any nucleotide ie N represents the four possible nucleotides in the DNA sequence: "A", "T", "C" and "G" for Adenine, Thymine, Cytosine and Guanine, respectively. As such, the degenerate probe sequences contain mixtures of various probes including all possible combinations of A, T, C and G at the "N" positions.

Please replace the paragraph at page 30, line 30 to page 31, line 3 as follows:

For example, exon 11 of the cystic fibrosis gene (CFTR) may be amplified using a nested PCR approach. For the first round, the following primers may be used:

~~5'-TGAAATAATGGAGATGCAATGTTC-3'~~

~~5'-GCACAGATTCTGAGTAACCATAAT3'~~

5'-TGAAATAATGGAGATGCAATGTTC-3' (SEQ ID NO.2); and

5'-GCACAGATTCTGAGTAACCATAAT3' (SEQ ID NO.3)

For the second round, the following primers may be used:

~~5'-CAACTGTGGTAAAGCAATAGTGT-3'~~

~~5'-TACCAAATCTGGATACTATAACCAT-3'~~

5'-CAACTGTGGTAAAGCAATAGTGT-3' (SEQ ID NO.4); and

5'-TACCAAATCTGGATACTATAACCAT-3' (SEQ ID NO.5)

Please replace the paragraph at page 37, lines 20-25 as follows:

Preferably, the amplifying of DNA from an isolated chromosome or a part of an isolated chromosome is randomly primed amplification. More preferably the randomly primed amplification includes the use of a degenerate oligonucleotide primer. Most preferably, the degenerate oligonucleotide primer consists of the nucleotide sequence 5'-CCGACTCGAGNNNNNATGTGG-3' 5'-CCGACTCGAGNNNNNATGTGG-3' (SEQ ID NO.1), wherein N is any nucleotide.

Please replace the paragraph at page 38, lines 8 –14 as follows:

Preferably, the amplifying of DNA from one or more cells with an unknown karyotype and the amplification of DNA from one or more cells with a reference karyotype is randomly primed DNA amplification. More preferably, the amplifying includes the use of a degenerate oligonucleotide primer. Most preferably, the degenerate oligonucleotide primer consists of the nucleotide sequence 5'-CCGACTCGAGNNNNNATGTGG-3' 5'-CCGACTCGAGNNNNNATGTGG-3' (SEQ ID NO.1), wherein N is any nucleotide.

Please replace the paragraph at page 47, lines 21-30 as follows:

Preferably, the one or more primers used is an oligonucleotide including one or more nucleotides of random sequence. More preferably, the one or more primers is an oligonucleotide including one or more contiguous nucleotides of random sequence. More preferably, the one or more of primers is an oligonucleotide that includes six or more contiguous nucleotides of random sequence, such as a DOP primer (degenerate oligonucleotide primer). Most preferably, the one or more primers is a primer with the following nucleotide sequence:

5'-CCGACTCGAGNNNNNATGTGG-3' 5'-CCGACTCGAGNNNNNATGTGG-3' (SEQ ID NO.1).

Please replace the paragraph at page 55, lines 24-29, as follows:

Preferably, the nucleic acids are derived from randomly primed amplification that includes the use of a degenerate oligonucleotide primer. More preferably, the nucleic acids are derived from randomly primed amplification that includes the use of a degenerate oligonucleotide primer that consists of the nucleotide sequence

5'-CCGACTCGAGNNNNNNATGTGG-3' 5'-CCGACTCGAGNNNNNNATGTGG-3' (SEQ ID NO.1), wherein N is any nucleotide.

Please replace the paragraph at page 58, lines 10-18, as follows:

Briefly, amplification was carried out in a Minicycler (MJ Research, USA) in a volume of 50 μ l, which contained about 50 ~100 ng of source probes, Taq DNA ploymerase buffer (50 mM KCl, 10 mM Tris-HCl [pH 8.3], Perkin Elmer, USA), 2.0 μ M primer 6MW(5'-CCGACTCGAGNNNNNNATGTGG-3' 6MW(5'-CCGACTCGAGNNNNNNATGTGG-3' (SEQ ID NO.1), 2.5 mM MgCl₂, 0.25mM of each dNTP, and 5 U Taq DNA polymerase (Perkin Elmer, USA). After an initial denaturation step of 95°C for 4 min, 30-35 cycles were followed using cycling conditions of 94°C for 1 min, 62°C for 1 min, and 72°C for 3 min with an addition of 10 seconds per cycle to the extension time. Finally an extension step of 72°C for 10 min was added at the end of cycling amplification.

Please replace the paragraph at page 74, lines 7-19, as follows:

100 ng of Cot-1 DNA (Cat. No., 15279-011, Invitrogen) was amplified using DOP-PCR in a Minicycler (MJ Resrarch, USA) in a volume of 50 μ l containing 5 U of *Taq* polymerase (Applied Biosystems), and a final concentration of 50 mM KCl, 10 mM Tris-HCl pH 8.3, 0.1 mg/ml gelatin, 2.5 mM MgCl₂, 200 μ M of each dNTP, 2 μ M DOP-PCR 6MW primer (5'-CCGACTCGAGNNNNNNATGTGG-3' (5' CGACTCGAGNNNNNNATGTGG-3' - SEQ ID NO.1) (Telenius et al. 1992). The sample was centrifuged briefly, denatured at 95°C for 5 min, and cycled for 8 cycles of: 94°C for 1 min, 30°C for 1.5 min, 72°C for 3 min with a ramp of 1°C per 4 seconds between the annealing and the extension steps, followed by 29 cycles of 94°C for 1

min, 62°C for 1 min, 72°C for 3 min initially, but increased by 14 seconds for each cycle, and a final extension step at 72°C for 10 min. 5 µl of amplified products was run on a 1% Agarose gel (Figure 11 top panel) and the rest purified.

Please replace the paragraph at page 75, line 29 to page 76, line 7 as follows:

(iii) First round of DOP-PCR for random amplification of single cells

First round of DOP-PCR was performed in a Minicycler (MJ Research, USA) in a volume of 50 µl containing the single-cell lysed and neutralized solution (10 µl), 5 U of *Taq* polymerase (Applied Biosystems), and a final concentration of 50 mM KCl, 100 mM Tris-HCl pH 8.3, 0.1 mg/ml gelatin, 2.5 mM MgCl₂, 200 µM of each dNTP, 2 µM DOP-PCR 6MW primer (*5'-CCGACTCGAGNNNNNNATGTGG-3'* (*5'-CCGACTCGAGNNNNNNATGTGG-3'* – SEQ ID NO.1) (Telenius et al. 1992). The sample was centrifuged briefly, denatured at 95°C for 5 min, and cycled for 8 cycles of: 94°C for 1 min, 30°C for 1.5 min, 72°C for 3 min with a ramp of 1°C per 4 seconds between the annealing and the extension steps, followed by 26 cycles of 94°C for 1 min, 62°C for 1 min, 72°C for 3 min initially, but increased by 14 seconds for each cycle, and a final extension step at 72°C for 10 min.

Please replace the Table 5. at page 85 as follows:

Table 5.

Primers used for amplification of 10 different DYS loci for both the preparation of probes for array printing and the preparation of single-cell targets for array CGH analyses using Selectively-Enhanced Primer-extension-preamplification (SEP)

Locus	Orientation	Primer sequences (5' → 3')	Products (bp)
DYS19	F	ATGTGGCGATCCTATT (<u>SEQ ID NO.6</u>)	3682
	R	TTGACAAGCCCAAAGTT (<u>SEQ ID NO.7</u>)	
DYS385	F	TGAGTCGTTAGAGGGCTTCC (<u>SEQ ID NO.8</u>)	4676
	R	AATCTACGGGCCACGCAT (<u>SEQ ID NO.9</u>)	
DYS389	F	TCCTAGGGATTAGGCCTTCAGTA (<u>SEQ ID NO.10</u>)	4244
	R	TGCATTAGCATGAGAGATCCTG (<u>SEQ ID NO.11</u>)	
DYS390	F	TGGTTCTAAATGAGGCCGAGG (<u>SEQ ID NO.12</u>)	3872
	R	TCGCTATGTGGGCCAGTCT (<u>SEQ ID NO.13</u>)	
DYS391	F	TTTTGACAATAGCCATTCCAG (<u>SEQ ID NO.14</u>)	4039
	R	ACCAACATTTCTACTAAGATAAGG (<u>SEQ ID NO.15</u>)	
DYS392	F	TTACAATTGAGAACCGGCTCCTG (<u>SEQ ID NO.16</u>)	3252
	R	TGGAGGCATCACACTACCTGAC (<u>SEQ ID NO.17</u>)	
DYS393	F	CATCTCCCAGGTTCAAGTGATTG (<u>SEQ ID NO.18</u>)	3454
	R	TTCGCACCAACATTCTCCATTCTG (<u>SEQ ID NO.19</u>)	
DYS437	F	AATGCACTCAGAGGACTGGACC (<u>SEQ ID NO.20</u>)	3043
	R	TGGAACCTATCTCCTGTTCATGTG (<u>SEQ ID NO.21</u>)	
DYS438	F	CTCGGACTCCTGACATCAAGTG (<u>SEQ ID NO.22</u>)	3153
	R	GAAACCGTGCATCTAACACCAG (<u>SEQ ID NO.23</u>)	
DYS439	F	GCTCAGAGTCATGGTTCCAGC (<u>SEQ ID NO.24</u>)	2054
	R	GCTGCATAAAGTGTACAGAGGCC (<u>SEQ ID NO.25</u>)	